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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,743	07/21/2003	David T. Hung	12.026011-DIV	4720

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,743	HUNG, DAVID T.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-20,25,26 and 29-40* is/are pending in the application.

4a) Of the above claim(s) *15,19,20 and 30-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,16-18,25,26 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Hung

1. Applicant's election of Group II (claims 14, 16 and 18) and species election of "nuclear mitotic spindle apparatus protein (NuMA)" in the reply filed on 5/30/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The information disclosure statement (IDS) filed on 7/21/03 has been considered. A signed copy is attached hereto.

3. Claims 13-20, 25, 26, and 29-40 are pending. Claims 1-12, 21-24, 27, and 28 are cancelled. Claims 15, 19, 20, and 30-40 are withdrawn from further consideration as being drawn to non-elected inventions.

4. Claims 13, 17, 25, 26 and 29 are linking claims. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the

provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. Claims 13, 14, 16-18, 25, 26 and 29 are under examination.

6. Due to species election, claims are examined to the extent that the nuclear matrix protein is nuclear mitotic spindle apparatus protein (NuMA).

Priority

7. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 and under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The "nuclear matrix protein" recited in the instant claims 13, 14, 16-18, 25, 26 and 29, and the "nuclear mitotic spindle apparatus protein" recited in claim 17 are not described in the provisional applications no: 60/117,281 and non-provisional application no. 09/313,463. Accordingly, the claims are given the priority date of the provisional application no. 60/166,100 (11/17/1999).

If applicant believes that support for claims 13, 14, 16-18, 25, 26 and 29 is present in the earliest filed priority document, applicant must, in responding to this action, point out with particularity, where such support may be found.

Specification

8. The first line of the specification should be updated if applicant desires priority under 35 U.S.C. 1 19(e), 120, 121 and 3654c) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application (s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No.___" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date 6f the parent application.

For additional information, see United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003) "Benefit of Prior-Filed Application".

Appropriate correction is required.

9. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code see page 2, line 32, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code found throughout the specification. See MPEP § 608.01.

Claim Objections

10. Claim 14 is objected to as it contains non-elected inventions. Appropriate correction is required.

11. Claim 16 is objected to as being a duplicate of claim 14. Appropriate correction is required.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 26 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 26 recites the limitation "ductal fluid samples" in claim 13. There is insufficient antecedent basis for this limitation in the claim. Claim 13 only recites “a ductal fluid sample”.

B. Claim 29 recites the limitation "the single lumen" in claim 13. There is insufficient antecedent basis for this limitation in the claim. Claim 13 only recites “a lumen”.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 13, 14, 16-18, 25, 26 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAMA (1973, 224(6): 823-827, IDS) in view of Love et al. (Lancet 1996, 348: 997-999, IDS), Hou et al. (Radiology, 1995, 195 (2): 568-569, IDS) and US Patent No. 6,287,790 B1 (Data of Patent: 9/11/2001, effective filing date 11/30/1998)

Claims 13, 14, 16-18, 25, 26 and 29 are drawn to a method for identifying a patient having breast cancer or breast precancer, said method comprising: placing a ductal access tool comprising a lumen in a breast duct of a patient; infusing a fluid into the duct through the lumen; retrieving a ductal fluid sample from the accessed duct through the lumen and examining the ductal fluid sample to determine the presence of a marker comprising an expression product of a gene encoding a nuclear mitotic spindle apparatus protein (NuMA). The claims are further limited wherein the expression product is a polypeptide, the step of examining comprises contacting the polypeptide with an antibody that specifically binds to the polypeptide, the fluid collected is from a single duct, the ductal fluid sample is collected from a plurality of ducts, the lumen has an inner diameter large enough to retrieve clusters of greater than 10 cells.

The JAMA reference teaches a method comprising inserting hair-like catheters into breast ducts, flushing the ducts with saline for cell studies and examining the fluid from each duct separately (see page 823, left column, 4th paragraph, and page 827, left column, 3rd paragraph). The JAMA reference teaches that the fluid sample contains usable cells (see page 826). The JAMA reference teaches that the fluids are tested for reverse transcriptase, an enzyme that has been implicated as a possible cancer marker (page 827, left column, 5th paragraph).

JAMA reference does not teach that the sample is collected from a plurality of ducts. JAMA reference does not teach detecting NuMA using an antibody. JAMA reference does not teach retrieving a ductal fluid sample from the accessed duct through the lumen. JAMA reference does not teach that the lumen has an inner diameter large enough to retrieve clusters of greater than 10 cells. However, these deficiencies are made up for in the teachings of Love, Hou and the US Patent No. 6,287,790 B1.

Love et al. teach a method of collecting ductal fluid from a breast comprising inserting a cannula (0.4 mm outer diameter) into one or more breast ducts, infusing saline into the breast ducts, collecting the washings from the ducts and analyzing the washings cytologically (see page 997, right column under methods). Love et al. teach that the ducts containing DCIS that were successfully cannulated gave rise to exfoliated DCIS cells which could be retrieved by washings and the cells were confirmed as DCIS cells by positive membrane neu immunoreactivity, positive nuclear p53 immunoreactivity or aneuploidy (see page 999, left column, 1st paragraph). Love et al.

that because the duct was so small that is difficult to aspirate back through a cannula to obtain material, the sample was collected externally in a capillary tube after removing the catheter, and this collecting method is not optimal and a double-lumen tube is being developed to overcome this difficulty (see page 998, right column, 2nd paragraph).

Hou et al. teach cannulation of a breast duct with a 0.7mm diameter, 1.9 cm long intravenous catheter, infusing s small volume of sterile, water soluble contrast material into the breast duct, and aspirating the contrast solution from the duct through the catheter (see page 568, middle column, last paragraph and right column, 1st paragraph). The catheter used by Hou (0.7 mm diameter) is large enough to retrieve clusters of greater than 10 cells.

US Patent No. 6,287,790 B1 teaches that NuMA can be used to identify tumor cells and different stages in the breast tumor progression and differentiation processes (see abstract). US Patent No. 6,287,790 B1 teaches that proliferating non-malignant and malignant mammary epithelial cells show significantly different nuclear distribution of NuMA protein (see Fig. 11). US Patent No. 6,287,790 B1 teaches detection of NuMA using a NuMA specific antibody (see abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of JAMA, Hou, Love and Patent '790 to arrive the instant invention. One would have been motivated to do so because JAMA, and Love teach method of diagnosing breast cancer by isolating a ductal fluid from one or more breast ducts by ductal lavage and further detecting a cancer marker in the isolated ductal fluid, Hou teaches retrieving the solution from the duct through the

catheter, and Patent ' 790 teaches that NuMA is a breast cancer marker that can be used to identify breast tumor cells and different stages in the breast tumor progression and differentiation processes. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to do so because JAMA and Love teaches the method of isolating ductal fluid by ductal lavage, Hou teaches a method for cannulation of a breast duct with a catheter, infusing a solution into the duct and aspirating the solution from the duct through the catheter and Patent' 790 teaches a method of detecting NuMA in breast epithelial cells using a NuMA specific antibody.

16. Claims 13, 14, 16-18, 25, 26 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No.6,221,622 B1 (data of patent: 4/24/2001, effective filing date at least 4/28/1998, IDS) in view of Love et al. (Lancet 1996, 348: 997-999, IDS) and US Patent No. 6,287,790 B1 (Data of Patent: 9/11/2001, effective filing date 11/30/1998)

The interpretation of claims 13, 14, 16-18, 25, 26 and 29 is set forth above (see paragraph 15).

US Patent No. 6,221,622 B1 teaches a method for obtaining cellular and non-cellular marker materials from a single milk duct of a breast comprising locating a single milk duct, introducing a washing fluid into the duct, collecting the washing fluid from the duct and analyzing the marker materials that may be presented in the fluid, wherein the cellular marker materials may comprise epithelial cells from the lining of the duct, and the non-cellular marker materials include proteins, peptides, and other chemical species

which may be secreted or otherwise released into a duct in response to a disease or other condition to be identified (see abstract and column 3). US Patent No. 6,221,622 B1 teaches that the collected fluid may be treated or analyzed in conventional way to identify the presence, amounts of any marker materials that may be present in the sample (see column 7, lines 5-10). US Patent No. 6,221,622 B1 teaches that the diameter of the single lumen is from 0.5 mm to 1.5 mm (see column 6, lines 18-22). Such lumen is large enough to retrieve clusters of greater than 10 cells.

US Patent No. 6,221,622 B1 does not teach that the sample is collected from a plurality of ducts. US Patent No. 6,221,622 B1 does not teach detecting NuMA using an antibody. However, these deficiencies are made up for in the teachings of Love and the US Patent No. 6,287,790 B1.

Love et al. teach a method of collecting ductal fluid from a breast comprising inserting a cannula (0.4 mm outer diameter) into one or more breast ducts, infusing saline into the breast ducts, collecting the washings from the ducts and analyzing the washings cytologically (see page 997, right column under methods). Love et al. teach that the ducts containing DCIS that were successfully cannulated gave rise to exfoliated DCIS cells which could be retrieved by washings and the cells were confirmed as DCIS cells by positive membrane neu immunoreactivity, positive nuclear p53 immunoreactivity or aneuploidy (see page 999, left column, 1st paragraph).

US Patent No. 6,287,790 B1 teaches that NuMA can be used to identify tumor cells and different stages in the breast tumor progression and differentiation processes (see abstract). US Patent No. 6,287,790 B1 teaches that proliferating non-malignant

and malignant mammary epithelial cells show significantly different nuclear distribution of NuMA protein (see Fig. 11). US Patent No. 6,287,790 B1 teaches detection of NuMA using a NuMA specific antibody (see abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US Patent No. 6,221,622, Love and Patent '790 to arrive the instant invention. One would have been motivated to do so because US Patent No. 6,221,622 and Love teach a method of diagnosing breast cancer by isolating a ductal fluid from one or more breast duct by ductal lavage and further detecting a cancer marker in the ductal fluid and Patent ' 790 teaches that NuMA is a breast cancer marker that can be used to identify breast tumor cells and different stages in the breast tumor progression and differentiation processes. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to do so because US Patent No. 6,221,622 and Love teaches the method of isolating ductal fluid by ductal lavage and Patent' 790 teaches a method of detecting NuMA in breast epithelial cells using a NuMA specific antibody.

17. Claims 13, 14, 16-18, 25, 26 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No.6,494,859 (data of patent: 12/17/2002, effective filing date 4/28/1998) in view of Love et al. (Lancet 1996, 348: 997-999, IDS) and US Patent No. 6,287,790 B1 (Data of Patent: 9/11/2001, effective filing date 11/30/1998)

The interpretation of claims 13-19 is set forth above (see paragraph 5).

US Patent No.6,494,859 teaches a method for obtaining cellular and non-cellular marker materials from a single milk duct of a breast comprising locating a single milk duct, introducing a washing fluid into the duct, collecting the washing fluid from the duct and analyzing the marker materials that may be presented in the fluid, wherein the cellular marker materials may comprise epithelial cells from the lining of the duct, and the non-cellular marker materials include proteins, peptides, and other chemical species which may be secreted or otherwise released into a duct in response to a disease or other condition to be identified (see claim 5 and column 3). Love teaches that the ductal fluid isolated from a single duct comprises clusters of cells of greater than 11 cells in an epithelial clump (see column 19, lines 6-8 and columns 20-21, example 6).

US Patent No6,494,859 does not teach that the sample is collected from a plurality of ducts. US Patent No. 6,494,859 does not teach detecting NuMA using an antibody. However, these deficiencies are made up for in the teachings of Love and the US Patent No. 6,287,790 B1.

Love et al. teach a method of collecting ductal fluid from a breast comprising inserting a cannula (0.4 mm outer diameter) into one or more breast ducts, infusing saline into the breast ducts, collecting the washings from the ducts and analyzing the washings cytologically (see page 997, right column under methods). The diameter of the cannula used by Love (0.4 mm) is large enough to retrieve clusters of greater than 10 cells. Love et al. teach that the ducts containing DCIS that were successfully cannulated gave rise to exfoliated DCIS cells which could be retrieved by washings and the cells were confirmed as DCIS cells by positive membrane neu immunoreactivity,

positive nuclear p53 immunoreactivity or aneuploidy (see page 999, left column, 1st paragraph).

US Patent No. 6,287,790 B1 teaches that NuMA can be used to identify tumor cells and different stages in the breast tumor progression and differentiation processes (see abstract). US Patent No. 6,287,790 B1 teaches that proliferating non-malignant and malignant mammary epithelial cells show significantly different nuclear distribution of NuMA protein (see Fig. 11). US Patent No. 6,287,790 B1 teaches detection of NuMA using a NuMA specific antibody (see abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US Patent No. 6,494,859, Love and Patent '790 to arrive the instant invention. One would have been motivated to do so because US Patent No. 6,494,859 and Love teach a method of diagnosing breast cancer by isolating a ductal fluid from one or more breast duct by ductal lavage and further detecting a cancer marker in the ductal fluid and Patent ' 790 teaches that NuMA is a breast cancer marker that can be used to identify breast tumor cells and different stages in the breast tumor progression and differentiation processes. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to do so because US Patent No. 6,494,859 and Love teaches the method of isolating ductal fluid by ductal lavage and Patent' 790 teaches a method of detecting NuMA in breast epithelial cells using a NuMA specific antibody.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

Hong Sang
Art Unit 1643
June. 8, 2006